

## **REMARKS/ARGUMENTS**

### **Claim Amendments**

By the present amendment, claims 1, 41, 49, 54, 56 and 57 have been amended to specify that the conditions suitable for hydrolysis and condensation of the precursor to a siliceous material comprise combining the organic polyol silane precursor with the one or more additives at a pH in the range of about 4 to about 11.5. Support for this amendment is found, for example, on page 16, line 26, and in claim 38, of the application as filed.

Claim 38 has been amended to remove the subject matter now incorporated into claim 1 and to add the expression "comprise combining the organic polyol silane precursor with the one or more additives" which enhance the readability of the claim.

The claim amendment has been made without prejudice and without acquiescing to any of the Examiner's objections. The Applicants submit that no new matter has been added to the claims as a result of these amendments and their entry is respectfully requested. The Applicants reserve the right to file the canceled subject matter in divisional patent applications.

The Official Action dated May 17, 2006 has been carefully considered. It is believed that the claims submitted herewith and the following comments represent a complete response to the Examiner's rejections and place the present application in condition for allowance. Reconsideration is respectfully requested.

### **Recordation of Substance of Telephone Interview with Examiner Peng**

In accordance with 37 CFR §1.113(b), the Applicants submit the following recordation of the substance of a telephone interview with the Examiner that occurred on August 1, 2006. The following information is to supplement the information provided on form PTOL-413 dated August 2, 2006, prepared by the Examiner.

Present at the interview were Examiner Peng, Patricia Folkins (agent for the Applicants) and inventors John Brennan and Michael Brook. There were no exhibits shown or demonstrations conducted during the interview. The merits of all of the currently rejected claims were discussed. Specific prior art that was discussed included Gill (J. Am. Chem. Soc., (1998), 120, 8587-8598), Nakanishi688 (US 5,009,688) and Nakanishi875 (US 5,624,875). The Examiner's principal argument was that the claims that currently stand rejected under 35 U.S.C. § 103(a) are obvious over the combination of Gill and Nakanishi688 or Gill and Nakanishi875 because Gill teaches that it is desirable to replace the alkoxy groups in an alkoxysilane sol gel precursor (as used in both Nakanishi688 and Nakanishi875) with glyceryl groups since Gill teaches that the use of polyglyceryl silicate (PGS) as a sol gel precursor enhances the reproducibility of the sol gel forming reaction. The Applicants' principal argument was that Gill does not teach the replacement of alkoxy groups with glyceryl groups on alkoxysilane precursor compounds as is done in the method of the present invention. This difference is significant because sol gel reactions with PGS do not produce the same reaction product as those performed with polyol modified silanes, therefore the reactivity of these two species is entirely different under the reaction conditions utilized in the method of the present invention. As a result of these discussions, the Examiner indicated that if we can provide experimental proof of the difference in reactivity between PGS and Applicants' polyol modified silanes by performing side by side comparison reactions under the conditions claimed in the present application, and if those specific conditions were specified in the claim, then he would reconsider the current obviousness objections to the selected claims of the present application. The Examiner would prefer to have time to consider any new data and arguments, therefore the Examiner requested that the Applicants file a Request for Continued Examination in the present application.

**Claim Objections**

**35 U.S.C. §102**

The Applicants acknowledge and appreciate the Examiner's withdrawal of the objection to claims 40, 48 and 50 under 35 U.S.C. §102(b).

**35 U.S.C. §103(a)**

1. The Examiner has maintained his objection to claims 1-5, 8-10, 38, 40-45 and 47-48 under 35 U.S.C. §103(a) as being obvious over Nakanishi688 (US 5,009,688) in view of Gill (J. Am. Chem. Soc., (1998), 120, 8587-8598). The Applicants, once again, respectfully traverse this objection.

According to MPEP §2143,

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

Further

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, not in the applicant's disclosure.

Nakanishi688 does not teach or suggest the use of compounds of Formula I in methods for preparing siliceous materials accordingly Nakanishi688 is only relevant to the present invention in respect of the use of water soluble polymers as an additive in such methods.

The Examiner, in his arguments on page 4, last paragraph, to page 5, second paragraph, correctly notes that the motivation or reason to modify a reference (in this

case Nakanishi688) may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by the Applicant (MPEP 2144). The Examiner goes on to state that the motivation or reason to combine Nakanishi688 with Gill is related to the reproducibility of the final products. The Examiner alleges that:

Gill teaches that by utilizing polyol (e.g. glyceryl groups) as the hydrolysable groups, reproducibility of the product is greatly improved.  
**Page 8488, left column.**

While the Examiner is correct that the motivation to combine references to arrive at a claimed invention need not be the same one that was relied on by the inventors, the courts held *In re Dillon* that

[t]he art provided the motivation to make the claimed compositions *in the expectation that they would have similar properties*. (Emphasis added)  
**919 F.2d at 693, 16 USPQ2d at 1901**

Therefore, for the Examiner's argument to be correct, there would have to be some evidence in the art that there is a reasonable expectation that the material used by Gill and that used by the Applicants would have similar properties. Accordingly, the Examiner's argument may have some merit if Gill taught the use of the same class of precursor as that used by the present Applicants. However, Gill does not teach exchanging alkoxy groups with glyceryloxy groups on a non-oligomeric silane. As stated on page 8488, left column, of Gill:

Here we provide an approach based on a novel class of biocompatible precursors, namely polyol esters of silicates and siloxanes, which addresses many of the above difficulties and permits the effective and reproducible fabrication of a diverse range of bio-doped sol-gel polymers. [Emphasis added]

Gill teaches the use of a partially hydrolyzed and condensed material (polyglyceryl silicate or PGS) as a precursor in the preparation of sol gels. This material is not equivalent to the monomeric alkoxysilanes utilized by the Applicants. The Applicants have confirmed this fact with experimental evidence. This evidence has been provided in the attached declaration of Michael A. Brook under 37 CFR §1.132 where the non-equivalence of polyglyceryl silicate and polyol silanes (specifically diglycerylsilane or DGS), as well as alkoxysilanes, has been proven by performing sol gel reactions under identical conditions and showing that these precursor compounds do not produce the same reaction product.

The Applicants performed sol gel reactions under equivalent conditions with diglycerylsilane (a precursor within the scope of the present invention), polyglyceryl silicate (the precursor used in Gill) and tetraethoxysilane (a precursor used in Nakanishi688). These reactions were performed near the extreme range of pH that is claimed in the present application (i.e at pH 5.5 and 11) under conditions otherwise commensurate in scope with Nakanishi688 in view of Gill as requested by the Examiner. The data clearly shows the significant difference between the reactivity and resulting products produced by these three precursors. The material of the present invention was the only one that produced macroporous siliceous materials under these conditions. Accordingly, with a view to better distinguish the methods claimed in the present application, the Applicant has amended all of the independent claims in the present application to specify that the "suitable reaction conditions" comprise combining the organic polyol silane precursor with the one or more additives at a pH in the range of about 4 to about 11.5. Neither Gill nor Nakanishi688 teach the desirability of this specific range of pH's for the preparation of siliceous materials using the precursor species taught therein.

The Applicants submit that the evidence presented in the attached declaration clearly shows that the polyol silane precursors of the present invention are not only novel over the teachings in the cited art, but that they are also non-obvious as a person skilled in the art would not have been motivated to modify Nakanishi688 to replace the

alkoxysilane precursors with polyol silane precursors in light of the teachings of Gill. This is because Gill teaches the use of already partially hydrolyzed and condensed precursor materials which (as proven by the Applicants' experiments) are not equivalent to the non-polymerized species used by the Applicants in particular under the reaction conditions claimed in the present application.

The Applicants further submit that there is absolutely no teaching in Gill or Nakanishi688 that would suggest that replacement of Nakanishi688's alkoxy groups with glyceryloxy groups would enhance the reproducibility of Nakanishi688's method. Although Nakanishi688 does suggest that oligomers of metal alkoxides could be used in the methods disclosed therein, all of the examples in Nakanishi688 are performed with monomeric metal alkoxides. Further a person skilled in the art would recognize that as a polymerization reaction proceeds, the reaction characteristics change significantly so that what occurs when a reactant (in this case, glycerol) is added part way down the reaction path is in no way predictive of what would happen if that reactant was added much earlier on (indeed in the present application, glycerol is not "added" during the preparation of a sol gel as it is already incorporated into the starting material). The Examiner suggests that, since Gill's polyglyceryl silicate is an intermediate when Applicants' polyol silane precursor is partially hydrolyzed and condensed, this provides implicit disclosure that would lead a person skilled in the art to replace Nakanishi688's lower alkoxy groups with glycerol groups (citing MPEP 2144.01). As stated in MPEP 2144.01:

[I]n considering the disclosure of a reference, it is proper to take into account not only specific teachings of the reference but also the inferences which one skilled in the art would *reasonably be expected to draw therefrom*. (Emphasis added) ***In re Prada*, 401 F.2d 825, 826, 159 USPQ 342,344 (CCPA 1968).**

In light of the fact that Gill uses different precursor materials from those taught in Nakanishi688 in the preparation of the sol gel materials, we submit that a person skilled in the art would have no reasonable expectation that the substitution of Gill's precursor

materials in the method of Nakanishi688 would provide any improvement in the reproducibility of the method of Nakanishi688. Accordingly we respectfully submit that the Examiner's proposed motivation for a person skilled in the art to make such a substitution is not reasonable. This has been further substantiated by the experiments performed by the Applicants and submitted herewith (*vide supra*).

It is clear from the above that the Examiner has not met his burden to find motivation to modify the prior art references and thereby render the present invention obvious. In particular, there is absolutely no motivation or suggestion for a person skilled in the art to substitute the polyol silanes of the present invention for the alkoxy silanes in the method of Nakanishi688, in particular in view of Gill. The Applicants have unequivocally shown that neither Gill's polyol silicates nor Nakinishi688's alkoxysilanes work in the method of the present invention.

Since in all of claims 1-5, 8-10, 38, 40-45 and 47-48, the use of organic polyol silanes is claimed, and, since neither Nakanishi688 or Gill teach the use of such precursors, and since the precursors utilized by Nakanishi688 and Gill have been proven to be non-equivalent, under the reaction conditions claimed in claims 1-5, 8-10, 38, 40-45 and 47-48, to the precursors of the present claims, the Applicants submit that the subject matter of claims 1-5, 8-10, 38, 40-45 and 47-48 is not obvious in light of Nakanishi688 in view of Gill.

In light of the above amendments and arguments, the Applicants request that the Examiner's objection to claims 1-5, 8-10, 38, 40-45 and 47-48 under 35 U.S.C. §103(a) be withdrawn.

2. The Examiner has maintained the objection to claims 1-5, 8-10, 40-45, 47-52, 54-55 and 56 under 35 U.S.C. §103(a) as being obvious over Nakanishi875 (US 5,624,875) in view of Gill (J. Am. Chem. Soc., (1998), 120, 8587-8598). The Applicants respectfully traverse this objection.

According to MPEP §2143,

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

Further

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, not in the applicant's disclosure.

Nakanishi875 does not teach or suggest the use of compounds of Formula I in methods for preparing siliceous materials accordingly Nakanishi875 is only relevant to the present invention in respect of the use of water soluble polymers as an additive in such methods.

Similar to as argued above, if the Examiner's objection is to be correct, there would have to be some evidence in the art that there is a reasonable expectation that the material used by Gill and that used by the Applicants would have similar properties in order for it to be obvious to a person skilled in the art to substituted Nakanishi875's alkoxysilanes with the polyol silanes of the present invention. Accordingly, the Examiner's argument may have some merit if Gill taught the use of the same class of precursor as that used by the present Applicants. However, Gill does not teach exchanging alkoxy groups with glyceryloxy groups on a non-oligomeric silane. As stated on page 8488, left column, of Gill:

Here we provide an approach based on a novel class of biocompatible precursors, namely polyol esters of silicates and siloxanes, which addresses many of the above difficulties and permits the effective and reproducible fabrication of a diverse range of bio-doped sol-gel polymers. [Emphasis added]

Gill only teaches the use of a partially hydrolyzed and condensed material (polyglyceryl silicate or PGS) as a precursor in the preparation of sol gels. This material is not equivalent to the monomeric alkoxysilanes utilized by the Applicants. The Applicants have confirmed this fact with experimental evidence. This evidence has been provided in the attached declaration of Michael A. Brook under 37 CFR §1.132 where the non-equivalence of polyglyceryl silicate and polyol silanes (specifically diglycerylsilane or DGS), as well as alkoxysilanes, has been proven by performing sol gel reactions under identical conditions and showing that these precursor compounds do not produce the same reaction product.

The Applicants performed sol gel reactions under equivalent conditions with diglycerylsilane (a precursor within the scope of the present invention), polyglyceryl silicate (the precursor used in Gill) and tetraethoxysilane (a precursor used in Nakanishi875). These reactions were performed near the extreme range of pH that is claimed in the present application (i.e at pH 5.5 and 11) under conditions otherwise commensurate in scope with Nakanishi875 in view of Gill as requested by the Examiner. The data clearly shows the significant difference between the reactivity and resulting products produced by these three precursors. The material of the present invention was the only one that produced macroporous siliceous materials under these conditions. Accordingly, with a view to better distinguish the methods claimed in the present application, the Applicant has amended all of the independent claims of the present application to specify that the "suitable reaction conditions" comprise combining the organic polyol silane precursor with the one or more additives at a pH in the range of about 4 to about 11.5. Neither Gill nor Nakanishi875 teach the desirability of this specific range of pH's for the preparation of siliceous materials using the precursor species taught therein.

The Applicants submit that the evidence presented in the attached declaration clearly shows that the polyol silane precursors of the present invention are not only novel over the teachings in the cited art, but that they are also non-obvious as a person skilled in the art would not have been motivated to modify Nakanishi875 to replace the

alkoxysilane precursors with polyol silane precursors in light of the teachings of Gill. This is because Gill teaches the use of already partially hydrolyzed and condensed precursor materials which (as proven by the Applicants' experiments) are not equivalent to the non-polymerized species used by the Applicants in particular under the reaction conditions claimed in the present application.

The Applicants further submit that there is absolutely no teaching in Gill or Nakanishi<sup>875</sup> that would suggest the desirability of replacing of Nakanishi<sup>875</sup>'s alkoxy groups with glyceryloxy groups. Although Nakanishi<sup>875</sup> does suggest that oligomers of metal alkoxides could be used in the methods disclosed therein, all of the examples in Nakanishi<sup>875</sup> are performed with monomeric metal alkoxides. Further a person skilled in the art would recognize that as a polymerization reaction proceeds, the reaction characteristics change significantly so that what occurs when a reactant (in this case, glycerol) is added part way down the reaction path is in no way predictive of what would happen if that reactant was added much earlier on (indeed in the present application, glycerol is not "added" during the preparation of a sol gel as it is already incorporated into the starting material). As stated in MPEP 2144.01:

[I]n considering the disclosure of a reference, it is proper to take into account not only specific teachings of the reference but also the inferences which one skilled in the art would *reasonably be expected to draw therefrom*. (Emphasis added) ***In re Prada*, 401 F.2d 825, 826, 159 USPQ 342,344 (CCPA 1968).**

In light of the fact that Gill uses different precursor materials from those taught in Nakanishi<sup>875</sup> in the preparation of the sol gel materials, we submit that a person skilled in the art would have no reasonable expectation that the substitution of Gill's precursor materials in the method of Nakanishi<sup>875</sup> would provide any improvement in the reproducibility of the method of Nakanishi<sup>875</sup>. Accordingly we respectfully submit that there is no motivation for a person skilled in the art to make such a substitution. This has been further substantiated by the experiments performed by the Applicants and submitted herewith (*vide supra*).

It is clear from the above that the Examiner has not met his burden to find motivation to modify the prior art references and thereby render the present invention obvious. In particular, there is absolutely no motivation or suggestion for a person skilled in the art to substitute the polyol silanes of the present invention for the alkoxysilanes in the method of Nakanishi875, in particular in view of Gill. The Applicants have unequivocally shown that neither Gill's polyol silicates nor Nakanishi875's alkoxysilanes work in the method of the present invention.

In light of the above amendments and arguments, the Applicants request that the Examiner's objection to claims 1-5, 8-10, 40-45, 47-52, 54-55 and 56 under 35 U.S.C. §103(a) be withdrawn.

3. The objection to Claim 38 under 35 U.S.C. §103(a) as being obvious over Nakanishi875 (US 5,624,875) in view of Gill (J. Am. Chem. Soc., (1998), 120, 8587-8598) and as evidenced by Barkin (US 3,374,103) has been maintained. The Applicants respectfully traverse this objection.

Claim 38 depends on claim 1 and specifies that the conditions suitable for the hydrolysis and condensation of the precursor to a siliceous material include aqueous solutions, with optional sonication to assist in dissolution. The Examiner has combined the teaching in Barkin that the pKa of acetic acid is 4.76 with the teaching in Nakanishi875 that hydrolysis/condensation of a silicone alkoxide is carried out in a 0.001 mol/l aqueous solution of acetic acid to conclude that the pH of the reaction medium in Nakanishi875 should fall within the range claimed in claim 38 (now in all of the claims) of the present application.

The Applicants submit that the arguments and evidence provided above that teachings in Nakanishi875 in view of Gill do not render the claims in the present application obvious (in particular claim 1 upon which claim 38 depends), apply to the Examiner's objection to claim 38 described above. In particular, the Applicants, in the

attached declaration of Michael A. Brook under 37 CFR §1.132, have shown that, within the pH that is claimed in the present application, the reaction of Gill's precursors under conditions commensurate in scope with those in Nakanishi875, does not provide the materials that are produced under the reaction conditions claimed in the present application. The Applicants note that the operable pH range for the method of the present application has been included in all independent claims in the present amendment.

Accordingly, the Applicants submit that claim 38 is not obvious over Nakanishi875 (US 5,624,875) in view of Gill (J. Am. Chem. Soc., (1998), 120, 8587-8598) and as evidenced by Barkin (US 3,374,103) and request that the Examiner's objection to this claim under 35 U.S.C. §103(a) be withdrawn.

The Examiner has maintained the objection to claims 53 and 57-61 under 35 U.S.C. §103(a) as being obvious over Nakanishi875 (US 5,624,875) in view of Gill (J. Am. Chem. Soc., (1998), 120, 8587-8598). The Applicants respectfully traverse this objection.

The Examiner contends that:

it would have been obvious to one of ordinary skill in the art at the time of the invention was made to encapsulate Gill's biomolecules in Nakanishi875 in view of Gill's matrix.

As argued above, the Applicant submits that the matrixes prepared in Gill, using polyol silicates as silica precursors, are in no way suggestive of the materials prepared using the methods of the present invention since polyol silicates do not work in the method of the present invention. Nakanishi875 goes no further to teach a person how to arrive at the methods of the present invention since Nakanishi875 does not teach or suggest using polyol silane precursors. Accordingly, a person skilled in the art could not

combine the teachings of Gill and Nakanishi<sup>875</sup> to arrive the methods claims in claims 53 and 57-61 of the present invention.

In light of the above arguments, the Applicants request that the Examiner's objection to claims 53 and 57-61 under 35 U.S.C. §103(a) be withdrawn.

The Applicants acknowledge and appreciate the Examiner's indication that claims 6-7, 11-17, 19, 21-37, 46 and 74 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The Applicants acknowledge and appreciate the Examiner's indication that claims 39 and 62-73 are allowed.

In view of the foregoing arguments and amendments, we respectfully submit that the application is in order for allowance and early indication of that effect is respectfully requested. Should the Examiner deem it beneficial to discuss the application in greater detail, the Examiner is invited to contact the undersigned by telephone at (416) 957-1683 at the Examiner's convenience.

Respectfully submitted,

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